2. Rejection of claims 1, 23, 41, 45, and 48-62 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1, 23, 41, 45, and 48-62 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent Nos. 5,695,953 and 5,981,701 (the Wallach patents), which the Action asserts have an effective priority date of September 12, 1988. In particular, the Action contends that the Wallach patents disclose the isolation of a TNF binding protein isolated from the urine of human patients, and that absent evidence to the contrary, this soluble TNF binding protein is identical to that of the protein of SEQ ID NO: 4 of the instant application. The Action also contends that although the claims of the instant application recite a recombinant polypeptide, there is no evidence that a recombinantly produced polypeptide would differ from the protein disclosed in the Wallach patents. The Action further contends that the Wallach patents disclose that the TNF binding protein isolated from the urine of human patients can be produced recombinantly.

To support a rejection under 35 U.S.C. § 102, "the four corners of a single, prior art document [must] describe every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation." *In re Paulsen*, 30 F.3d 1475, 1479 (Fed. Cir. 1994). The exclusion of even a single claimed element from a reference, no matter how insubstantial or obvious, is enough to negate anticipation. *Connell v. Sears, Roebuck & Co.*, 220 U.S.P.Q. (BNA) 193, 198 (Fed. Cir. 1983). The identical invention must also be shown in the single prior art reference in as complete detail as contained in the application against which the reference is cited. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989). Moreover, the disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. M.P.E.P § 2121.01; *Elan Pharm., Inc. v. Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 1054 (Fed. Cir. 2003); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 88 (D. Mass 2001) (citing *Akzo N.V. v. United States Int'l Trade Comm'n*, 808 F.2d 1471, 1479 (Fed. Cir. 1986)). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. M.P.E.P § 2121.01. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re*

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, Illinois 60606
312-913-0001

Donohue, 766 F.2d 531 (Fed. Cir. 1985).

Applicants note that the Wallach patents provide only a *partial, incomplete* amino acid sequence of a TNF inhibitory protein – and no nucleotide sequence whatsoever (*see* col. 4, ln. 27-31; col. 10, ln. 43-46; and col. 12, ln. 32-37 of the '953 patent; Applicants note that U.S. Application No. 08/474,691, from which the '701 patent issued, is a divisional of U.S. Application No. 07/876,828, from which the '953 patent issued). Applicants contend that because the Wallach patents do not disclose the complete nucleotide and amino acid sequence of TNF binding protein – and in fact, disclose *only* fourteen of the first sixteen amino acid residues of a TNF inhibitory protein – this reference *cannot* anticipate methods for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a therapeutically effective amount of a recombinant polypeptide having the ability to bind TNF, wherein said polypeptide is encoded by a nucleic acid molecule comprising the nucleotide sequence as set forth in SEQ ID NO: 3, or comprises the amino acid sequence as set forth in SEQ ID NO: 4. There is no evidence in the Wallach patents that the small fragment for which sequence has been disclosed has the ability to bind TNF, a recited limitation of the instantly-claimed methods. The lack of such evidence in the reference precludes application of these references in support of the asserted anticipation rejection.

Applicants also note that the Wallach patents disclose a TNF binding protein purified from human urine by use of dialysis, ion exchange chromatography, and reverse phase high pressure liquid chromatography. Applicants contend that because the TNF binding protein disclosed in the Wallach patents is purified from urine, these references *cannot* anticipate methods that use a *recombinant* polypeptide having the ability to bind TNF. In particular, Applicants contend that, in light of the specification's teachings and knowledge in the art, one of ordinary skill in the art would readily understand that a *substantially* homogeneous TNF binding protein purified from urine would *not* be free of human urinary proteins, and that the recombinantly produced TNF binding protein of Applicants' invention must be *inherently* free of human urinary proteins. Only Applicants' invention provided the nucleic acid sequence of TNF binding protein, which was absolutely necessary, in order to recombinantly produce TNF binding protein. Moreover, Applicants contend that the assertion that methods that use a purified TNF binding protein anticipate methods that use a recombinant TNF binding protein is entirely analogous to the assertion, made in *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, that erythropoietin purified from patients with anemia anticipates recombinant

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, Illinois 60606
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erythropoietin. 126 F. Supp. 2d 69, 88 (D. Mass 2001) (holding that a reference disclosing erythropoietin purified from patients with anemia does *not* anticipate claims to recombinant erythropoietin).

Because the Wallach patents fail to disclose the nucleic acid sequence of TNF binding protein, these references fail to put a recombinant TNF binding protein into the public's possession, and thus, do not contain an enabling disclosure with respect to a recombinant TNF binding protein. In fact, the Wallach patents do nothing more than merely recite that a TNF binding protein isolated from human urine can be recombinantly produced. And yet, one of ordinary skill in the art, lacking the nucleic acid sequence of TNF binding protein, could not produce a recombinant TNF binding protein without undue experimentation. Applicants, therefore, contend that the Wallach patents cannot anticipate the claimed methods of the present application, and therefore, respectfully request that the rejection of claims 1, 23, 41, 45, and 48-62 on 35 U.S.C. § 102 grounds be withdrawn.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner O'Hara believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: November 23, 2005

By: _____
Donald L. Zuhn, Jr., Ph.D.
Reg. No. 48,710

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, Illinois 60606
312-913-0001